AMENDMENTS TO THE SPECIFICATION:

Immediately below the Title, please insert the following paragraph:

Cross-Reference To Related Applications

This application is the national stage application of PCT Patent Application No. PCT/US2003/36634, filed November 13, 2003, which claims priority to U.S. Provisional Application No. 60/426,256, filed November 13, 2002.

Please replace the paragraph spanning page 7, line 28 to page 8, lines 16 of the specification as originally filed with the following paragraph amended as indicated below:

All nucleotides (nt) and amino acid numbers refer to the location within the genotype 1b Con1 full-length HCV genome (Genbank Accession no. AJ238799; SEQ ID NO:27) commencing with the core-coding region. This sequence was assembled from chemically synthesized DNA oligonucleotides in a step-wise PCR assay essentially as described previously (5). Briefly, 10-12 gel-purified oligonucleotides (60-80 nt in length) with unique complementary overlaps of 16 nt were used to synthesize cDNAs spanning 600-750 bases. The final PCR products were purified, digested with appropriate restriction enzymes, and ligated into the similarly cleaved pGEM3Zf(+) plasmid vector (Promega). Multiple recombinant clones were sequenced, correct clones identified and overlapping cDNA fragments assembled into the contiguous genomic sequence: 5'NTR-C-E1-E2-p7-NS2-3-4A-4B-5A-5B-3'NTR (pHCVBMFL). The selectable replicon, pHCVrep1bBartMan/AvaII {SG-Neo (wt); Fig. 1} and the derivatives, pHCVrep1b/BBVII {SG-Neo (S2204I)} and pHCVrep1b/BBI {SG-Neo

(5AΔ47)}, containing the NS5A adaptive mutations, S2204I and an in-frame deletion of 47 amino acids (Δ47aa) between nt 6960 and 7102, respectively, have been described (5) (Fig. 1). The plasmid pHCVBMFL/S2204I {FL (S2204I); Fig. 1} contains the full-length genome with the NS5A adaptive change S2204I. For the genomic and subgenomic constructs, NS5B polymerase defective derivatives were generated carrying a triple amino acid substitution, changing the Gly-Asp-Asp (GDD) motif in the active site to Ala-Ala-Gly (AAG) (5), and throughout this report are referred to as pol-.

Please replace the paragraph on page 12, lines 1-15 of the specification as originally filed with the following paragraph amended as indicated below:

Total cellular RNA was isolated using TRIzol reagent (Gibco-BRL) according to the manufacturer's protocol. One-tenth of each RNA sample was used to quantify HCV-specific RNA levels using an ABI PRISM 7700 Sequence Detector (Applied Biosystems). Real time reverse transcription (RT)-PCR amplifications were performed using the TaqMan EZ RT-PCR core reagents (Applied Biosystems) and primers specific for the HCV 5' NTR: 5'-CCTCTAGAGCCATAGTGGTCT-3' (SEQ ID NO: 1) (sense, 50 μM), 5' CCAAATCTCCAGGCATTGAGC-3' (SEQ ID NO: 2) (antisense, 50 μM) and FAM-CACCGGAATTGCCAGGACGACCGG (SEQ ID NO: 3) probe, 10 μM; (Applied Biosystems). RT reactions were incubated for 30 min at 60°C, followed by inactivation of the reverse transcriptase coupled with activation of *Taq* polymerase for 7 min at 95°C. Forty cycles of PCR were performed with cycling conditions of 15 sec at 95°C and 1 min at 60°C. Synthetic HCV

RNA standards of known concentration were included with each set of reactions and used to calculate a standard curve. The real time PCR signals were analyzed using SDS v1.6.3 software (Applied Biosystems).

Please replace the Table on page 25, lines 1-15 of the specification as originally filed with the following paragraph amended as indicated below:

Table 1. Oligodeoxynucleotides used in this study.

Name	Sequence (SEQ ID NO)
885	(-)CCCTCTAGAACGCCCCGAAACCTAGGGTGGCG (SEQ ID NO:4)
1030	(-)CCCTCTAGACTCGAGGGAATTTCCTGGAC (SEQ ID NO:5)
1184	(+)GACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCA GCTCATCAGCTGACCAGCTGTCTGCGCCTTCC (SEQ ID NO:6)
1287	(+)AGACCGTGCACCAGACCACAACGGTTTCCCTCTAGCGGGATCAATTCCG (SEQ ID NO:7)
1288	(-)CCAGTAACGTTAGGGGGGGGGGAGGGAGAGGGGCGGAATTGATCCCGCT (SEQ ID NO:8)
1289	(+)CCAAAGGGCGCGCCATGCAGATCTTCGTGAAGACC (SEQ ID NO:9)
1290	(-)AATAGGAGCTCCACCGCGGAGACGC (SEQ ID NO:10)
1291	(+)CGGTGGAGCTCCTATTACGGCCTACTCCCAAC (SEQ ID NO:11)
1292	(-)ATTGGTGTACATTTGGGTGATTGG (SEQ ID NO:12)
1293	(+)TCTGGAAGCTTCTTGAAGACA (SEQ ID NO:13)
1294	(-)GGCTTGACGTCCTGTGGGCGGCGGTTGGTGTTACGTTTGGTTTTTCTTTGAGGTTTA GGATTCGTGCTCATTATTATCGTGTTTTTCAAAGG (SEQ ID NO:14)
1319	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCAGCTCATCA GCTGTACAGCTGTCTGCGCCTTCC(SEQ ID NO:15)
1320	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCAGCTCATCA GCTGCCCAGCTGTCTGCGCCTTCC(SEQ ID NO:16)
1322	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCAGCTCATCA GCTTACCAGCTGTCTGCGCCTTCC(SEQ ID NO:17)
1324	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCAGCTCATCA GCTGAACAGCTGTCTGCGCCTTCC(SEQ ID NO:18)

1325	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGGCCAGCTCATCAGC TACACAGCTGTCTGCGCCTTCC(SEQ ID NO:19)
1326	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCTCCTTGACCAGCTCATCAGC TATCCAGCTGTCTGCGCCTTCC(SEQ ID NO:20)
1327	(+)AGACGGCTAAGCGTAGGCTGGCCAGGGGATCTCCCCCCCCCCTTGACCAGCTCATCAGC TATCCAGCTGTCTGCGCCTTCC(SEQ ID NO:21)
1356	(-)CCGCTCTAGATACGTGATGGGGGCACCCGTGGTGATGGTCCTTACCCCGATTCTGATGT TAGGGTCGATAC(SEQ ID NO:22)
1358	(+)CCGATGTACACCAATGTGGACCAGGACCTCGTCGGCTGGCGAGCGCCCCCCGGGGCGC GTTCC(SEQ ID NO:23)
1359	(+)CCGCGTGCACCCGAGGGGTTGCGAAGGCGGTGGACTTTGTACCCGTCGAGTCTATGGG AACCACTATGCGGTCCCCGGTC (SEQ ID NO:24)
5'Ala	(+)CCACGCTAAGCGTAGGCTGGCCAGGGGAGCACCCCCCTCCTTGGCCAGCTC (SEQ ID NO:25)
5'Asp	(+)CCACGCTAAGCGTAGGCTGGCCAGGGGAGATCCCCCCTCCTTGGCCAGCTC (SEQ ID NO:26)

[a]Nucleotide changes are highlighted in bold and the resultant codon is underlined
[b]Restriction sites used for cDNA cloning are underlined
[c]The polarities of oligonucleotides are indicated either the HCV genome RNA sense (+) or its complement (-)